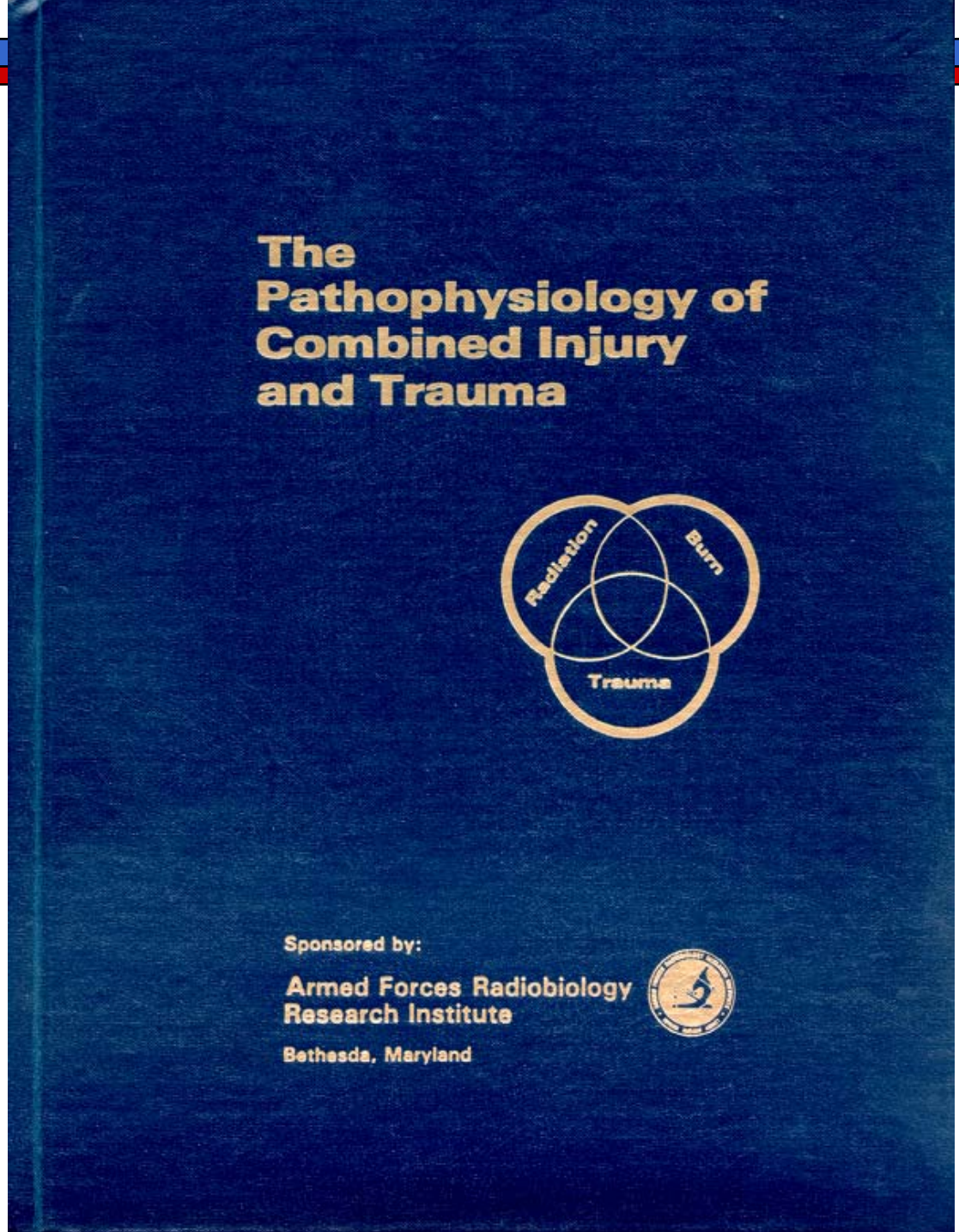
Combined Injury: Radiation in Combination with Trauma, Infectious Disease, or Chemical Exposures

Terry C. Pellmar, Ph.D.

AFRRI

UNIFORMED SERVICES UNIVERSITY
of the Health Sciences
Armed Forces Radiobiology Research Institute



AFRRI-sponsored International Conference on Combined Injury

April 27-29, 1983

"Over 100 physicians and scientists gathered to focus on the complex problems engendered by injuries of a combined nature"

Combined Injury

- Radiation + burns or wounds
- Radiation + infectious disease
- Radiation + chemical agents

Radiation + Trauma

Combined Injury: Radiation + Trauma

Predicted Injuries in a Major Radiation Event

Single injuries: 30- 40%

- Ionizing Radiation (including fallout)……. 15- 20%
- Burns…… 15%
- Wounds…..…… Up to 5%

Combined injuries: 65-70%

- Burns + wounds and irradiation…….. 20%
- Burns & irradiation…….. 40%
- Wounds and irradiation…… 5%
- Wounds and burns…….. 5%

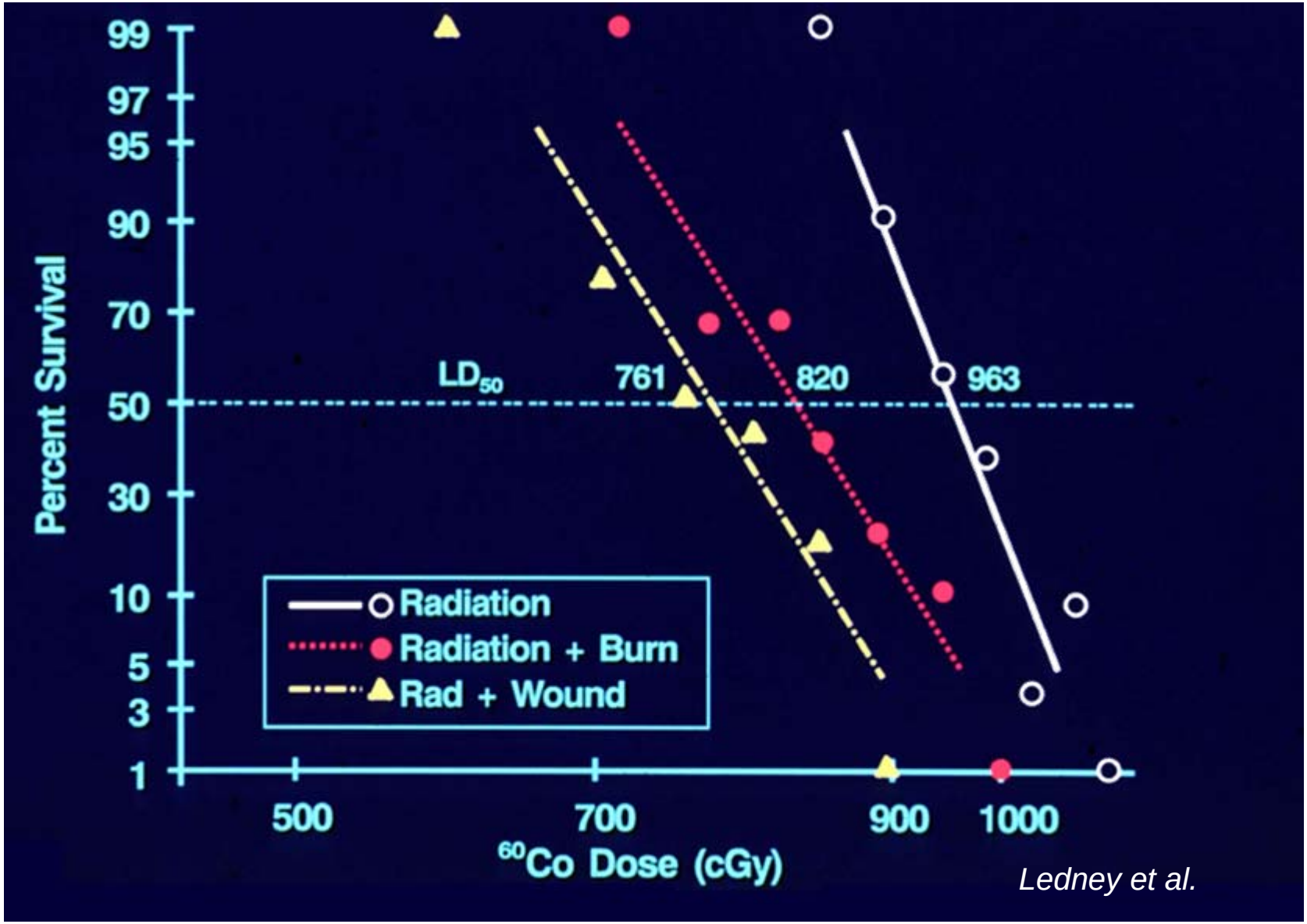
Combined Injury – A unique condition

- Federov: “radiation-burning trauma” is a new disease that differs significantly from both radiation and burn injuries
- Chromov et al: various traumas may amplify each other or they may lead to a completely different clinical picture
- Combined Injury modifies effects of therapeutic drugs

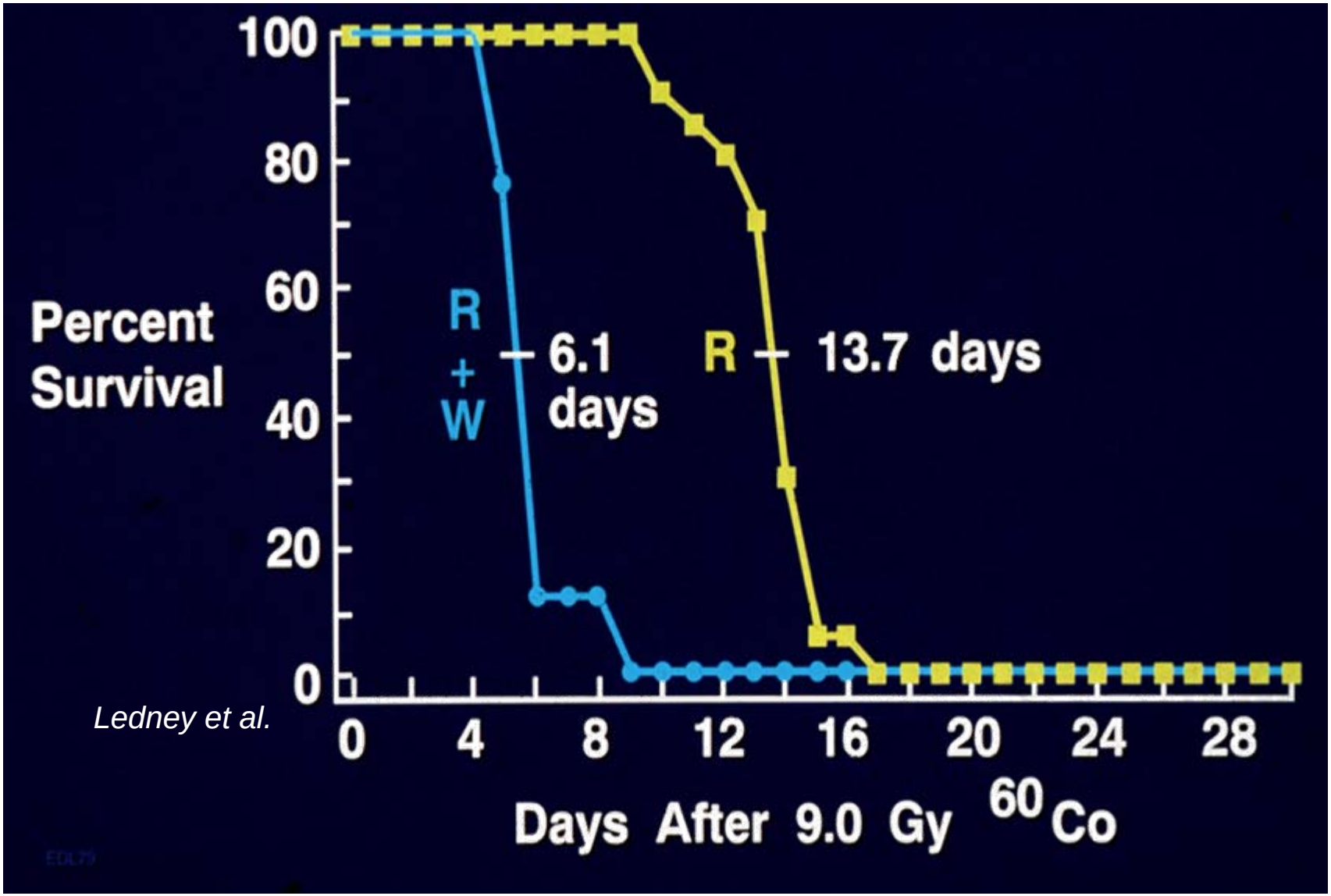
P38-39 Messerschmidt in Symposium Report

Combined Injuries in Swine at Nuclear Test Site

Radiation + Trauma: Increased Mortality



Radiation + Wounds: Reduced Survival Time

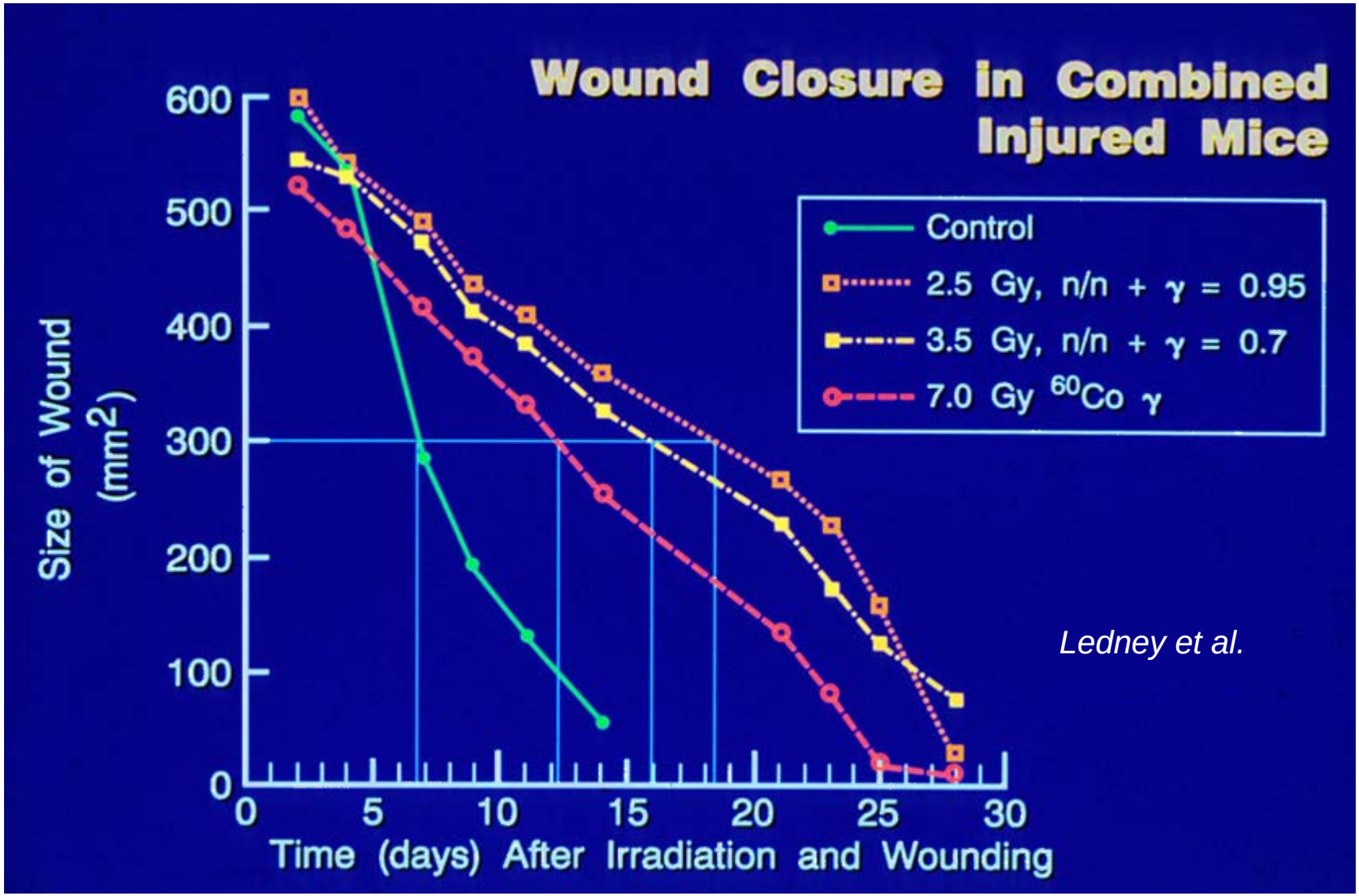


Ledney et al.

Survival after Combined Injuries: Complexities

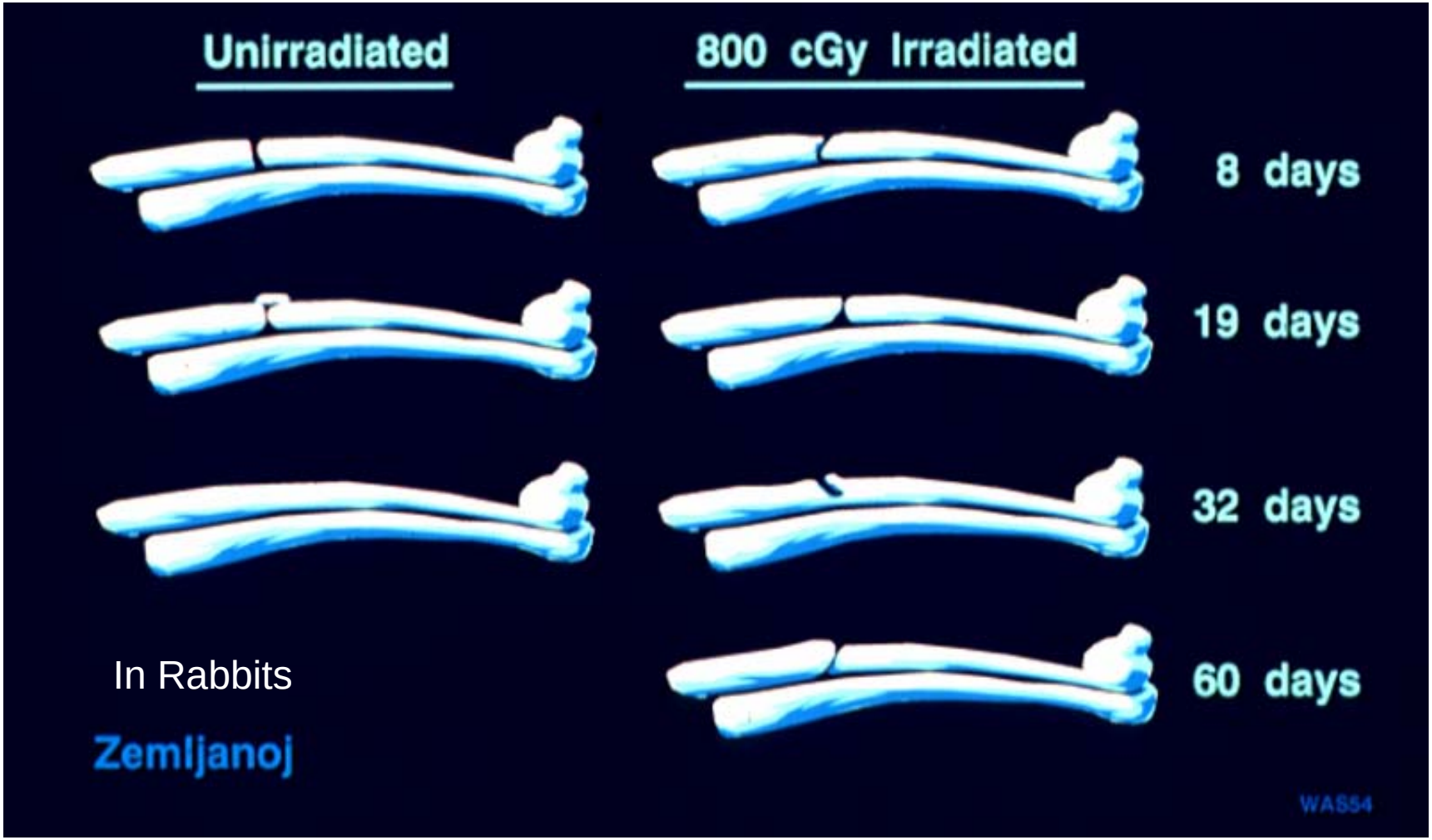
- Timing of trauma with radiation
  - Trauma prior to or concurrent with radiation can reduce mortality
  - Trauma after radiation significantly increases mortality
- Kind of injury
  - Burns, wounds, compressive injury elicit different patterns of mortality from combined injury

Wound Healing



Ledney et al.

Healing of Bone Fractures



Observations in Hiroshima
Gen Baku Sho – Atom Bomb Disease

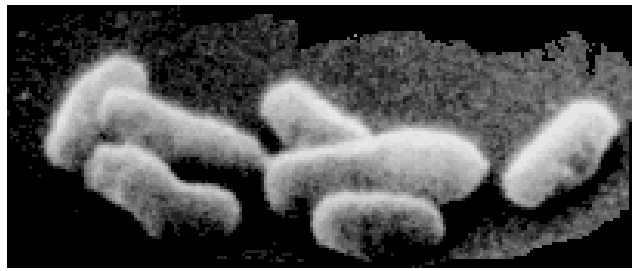
Wounds and burns seemed to heal initially but there was a serious relapse after 1-2 weeks.

- Late hemorrhaging of wound
- Bacterial infiltration of wounds
- Increased areas of necrotic tissue

Radiation - Infection Synergy

Radiation

+



Infectious agents

=

Increased mortality and morbidity

Radiation + Infection

- Exposure to ionizing irradiation increases susceptibility to bacterial and viral infections
  - immune response is impaired - limited white blood cells to fight infection
  - epithelial cell layers are compromised - normally barriers to infection
    - intestinal tract
    - lung
    - skin

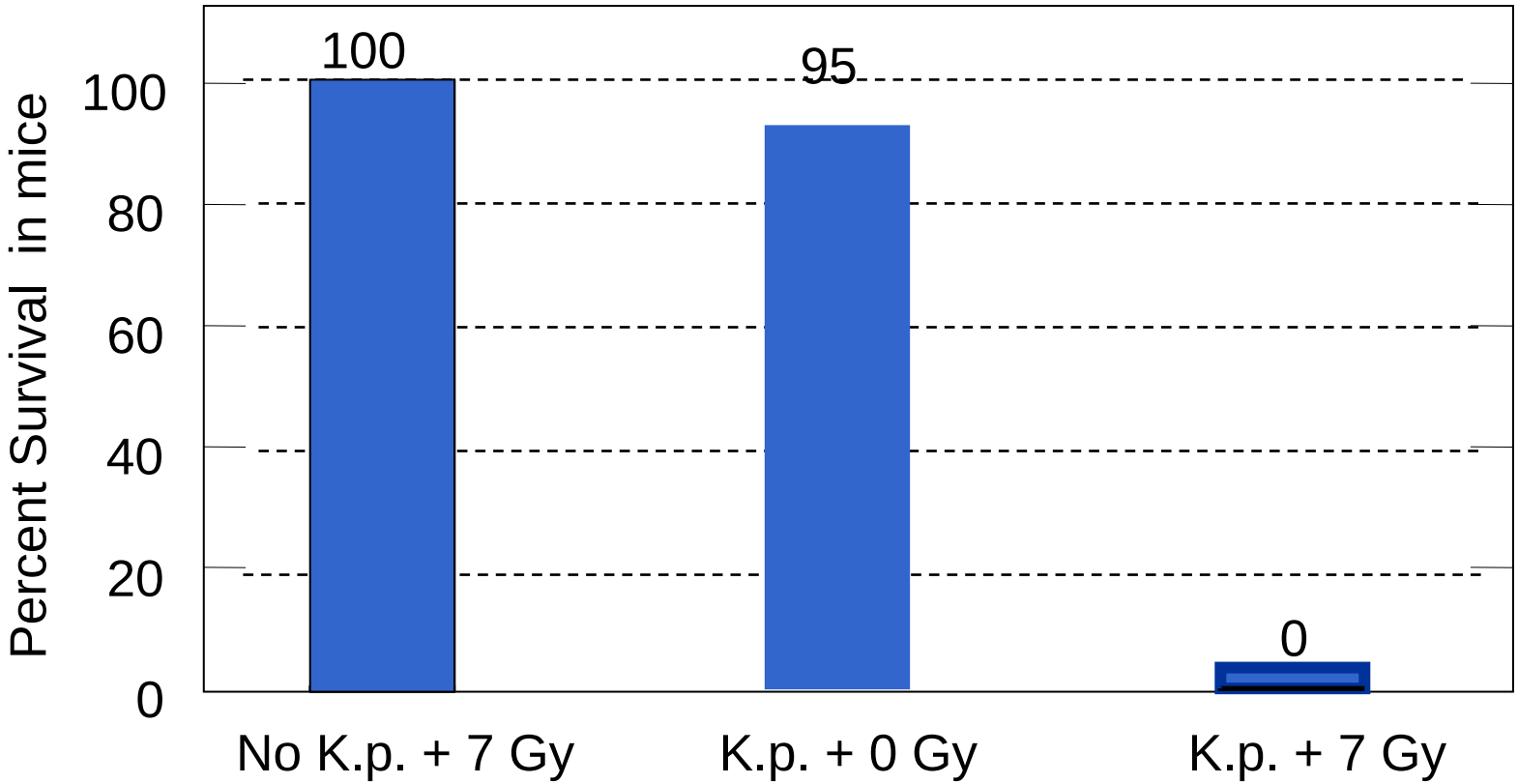
Likelihood of Combined Exposures

Infectious Disease with Natural Disasters		
	Hurricane Katrina	Tsunami
Population considered	1055	1354
Respiratory disease	<1%	97%
Diarrheal disease	95%	3%
Wound infection	5%	?

Number of patients was relatively low.

Chronic illnesses and pre-existing disease were concerns.

K. pneumoniae: a Pulmonary Infection

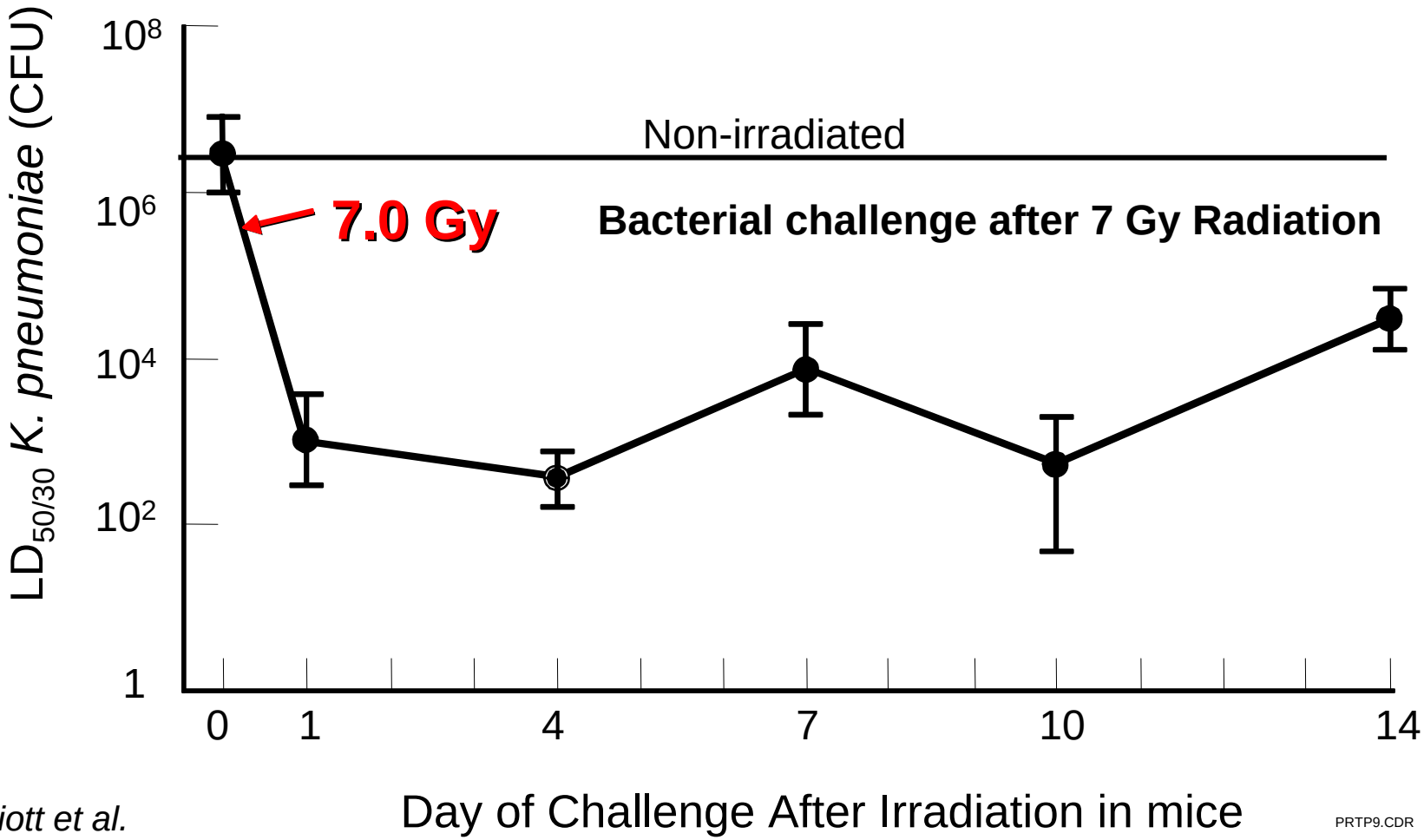


K.p. = Injection with 1.1 x 10^5 cells of *Klebsiella pneumoniae*

PRGK5.DRW

Elliott et al.

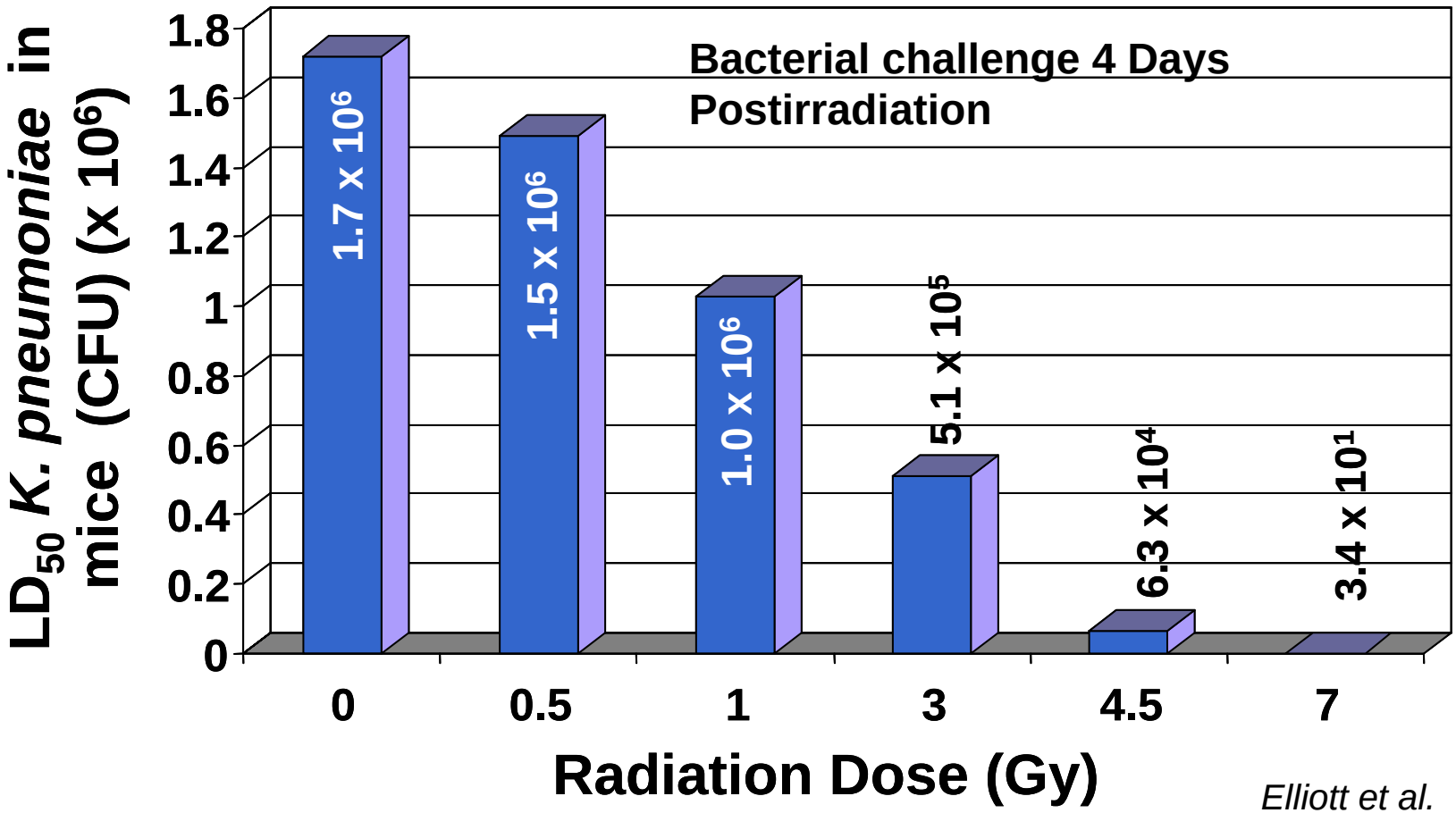
Radiation+ Infection: Time Course



Elliott et al.

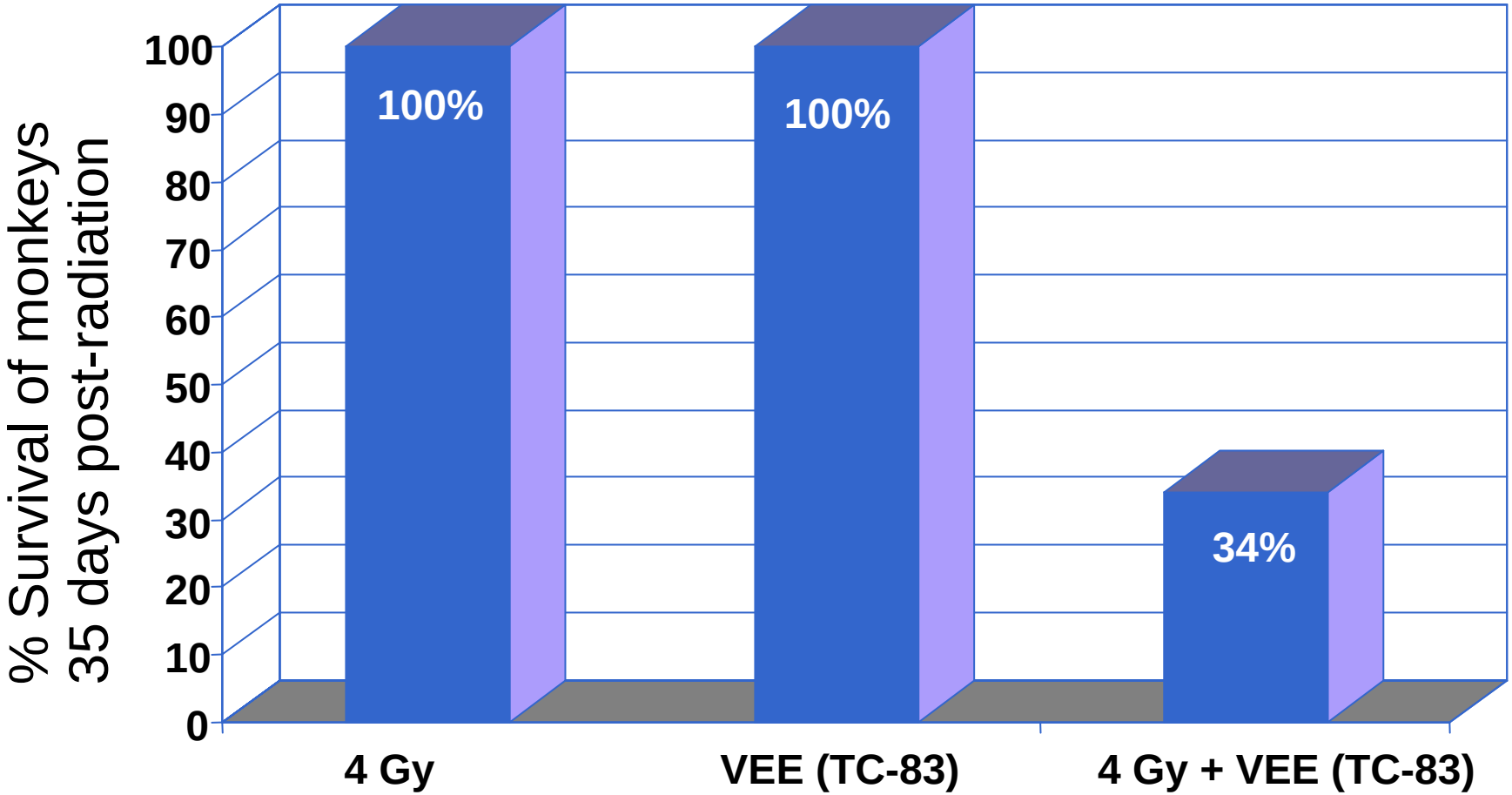
PRTP9.CDR

Radiation+ Infection: Effect of Radiation Dose



Elliott et al.

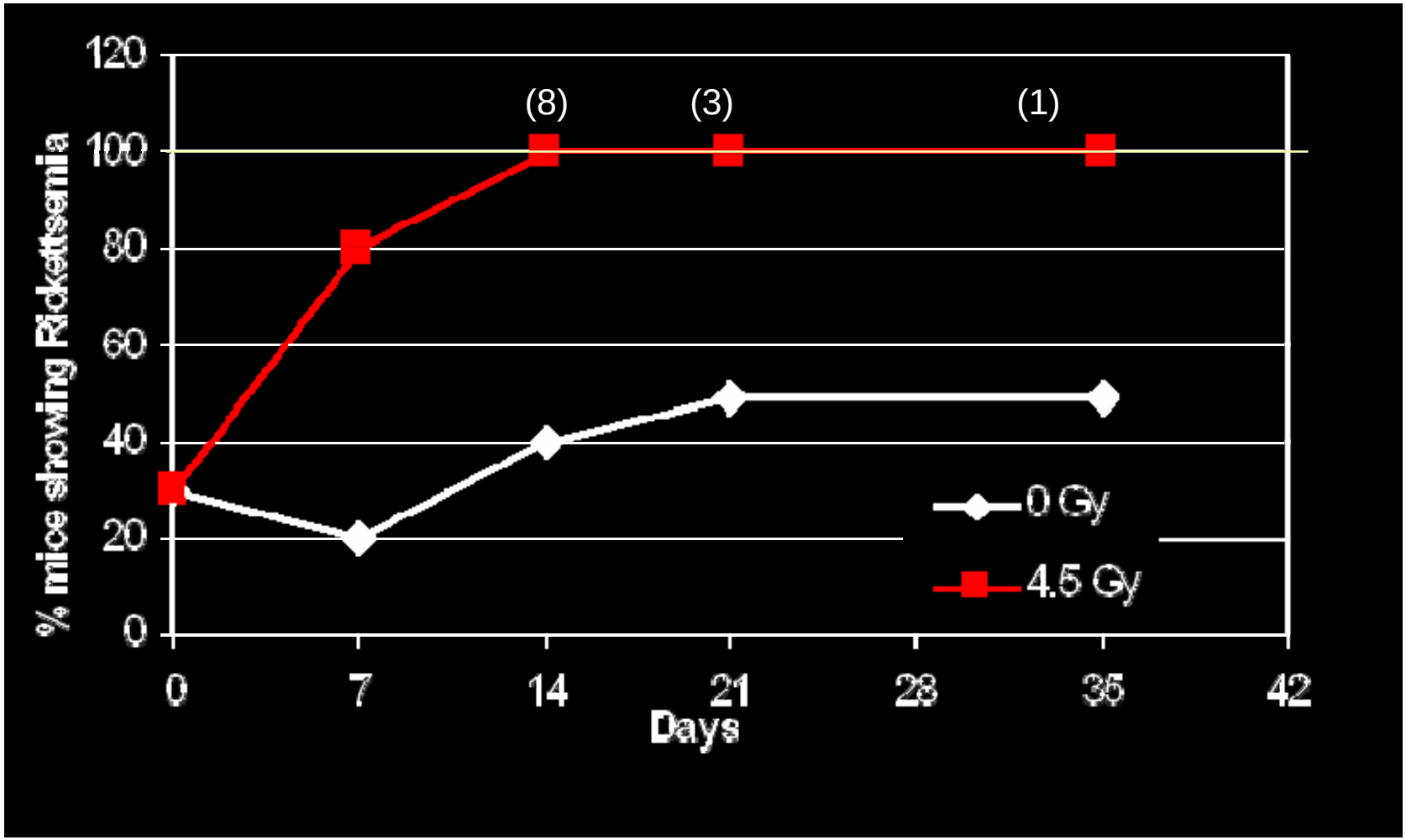
VEE: viral infection



VEE = 5 x 10^4 PFU s.c. into rhesus monkeys, 14 days postirradiation

Adapted from: Hilmas and Spertzel. 1975. Infect. Immun. 12:592-601.

Rickettsiae: a Latent Infection



Radiation exposure one year after an initial infection with Rickettsiae.

Kelly and Reese (1986) Infection and Immunity 52: 718-724.

Radiation + Chemicals

Likelihood of Combined Exposures: Chemicals

Some Chemicals Stored Near New Orleans

- Chlorine
- Ammonia
- Propane
- Methyl Ethyl Ketone
- Styrene
- Phenol
- Ethylene Glycol
- Trimethylbenzene
- Methanol
- Hexane
- Xylene
- Propylene
- Toluene
- Benzene
- Naphathalene
- Butane

Gasoline related products (e.g., benzene, toluene) were found in the water after Katrina

Examples of Reported Synergism

- Radiation + sodium nitrite increased translocations in mouse spermatocytes (Sushko and Malenchenko 1992)
- Radiation enhanced urethan-induced tumorigenisis in athymic mice (Kobayashi et al., 1996)
- Benzene + radiation greatly increased chromosomal aberrations in cultured human leukocytes (Igaku, 1976)

Conclusion

Combined injury is different from radiation injury alone.

New approaches are needed!